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A platform trial for patients with relapsed malignant mesothelioma

Submission date
22/08/2024

Recruitment status
Not yet recruiting

Registration date
04/11/2024

Overall study status
Ongoing

Last Edited
29/05/2025

Condition category
Cancer

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Mesothelioma is a rare cancer caused by exposure to asbestos typically affecting the lungs, the sac containing the heart and less commonly the lining of the abdominal cavity or testis. The prognosis for patients with relapsed mesothelioma is poor and the current treatment options are limited. It is thought that the outcome of the treatment is determined by the underlying genetic make-up of the cancer. For example, cancers with a mutation removing BAP1 have a much better prognosis compared with cancers with a mutation removing MTAP.
The SELECTmeso trial platform has been developed to gain insight into how beneficial targeting the genetic make-up of the cancer is. It is hoped that the outcome of this platform will justify future randomised trials to compare the effectiveness of targeted agents against standard of care.
The SELECTmeso trial platform aims to start recruitment in Winter 2025 with its first single-arm phase II trial SELECTmeso1. Further treatment arms will be added over time for specific targeted therapies.

Who can participate?
Patients aged 18 years and over with relapsed malignant mesothelioma

What does the study involve?
Patients will enrol into the trial platform by providing their diagnostic tumour sample which will be analysed in a laboratory to determine the genetic make-up of the cancer. The patient will be assessed for eligibility against the open treatment arms and offered to participate if eligible. Each arm will be looking at how well the treatment controls the disease after 12 weeks and 24 weeks. The researchers will also look at how long the patient is progression-free for, the safety of the treatment and how well it is tolerated by the patients.
Patients enrolling to SELECTmeso1 will received treatment with BMS-986504 for 6 months. This will involve taking 600mgs 4 times a day continuously in 3 weekly cycles and attending hospital visits for assessments, scans and blood tests.

What are the possible benefits and risks of participating?
The main risks are the potential side effects from the drug, BMS-986504, as outlined in the patient information sheet. This drug has been tested in humans before, so the side effects are

known but we are trying to find the ideal dose for this group of patients. Side effects for patients may include decreased appetite, nausea, diarrhoea, vomiting, skin issues (rash, itching or dry skin), fatigue and changes in some blood chemistry which in previous trials have all shown to be reversible. Patients will be encouraged to discuss these risks with their doctor/research team. The patients will be monitored on an ongoing basis to assess any side effects of the treatment.
During the study blood will be collected from the patients for biochemistry tests and research blood samples. The research blood samples are additional to standard of care for this patient group. Blood will be collected from a vein, which may cause pain where the needle is inserted. There is a small risk of bruising or infection at the site of insertion. Some individuals may experience dizziness, nausea or fainting when the blood is collected. Patients will be monitored closely and steps taken to minimise this.
There will be a total of five CT scans in this study, which is the same number as would be done in standard of care. There is an extremely small risk that the ionising radiation used in these procedures may cause cancer many years or decades after the exposure. The procedures will involve a liquid (contrast) being injected which can cause a warm/unpleasant sensation for a few minutes. A very small number of individuals react to the contrast.
The patients will be given the option to consent to a tissue biopsy if their disease progresses. There is a risk that the site of the incision may be inflamed. A CT scan or an ultrasound may be used to guide the health care professional to the area of disease. If this occurs then there is a small risk from the radiation, as explained above.

Where is the study run from?
University of Southampton (UK)

When is the study starting and how long is it expected to run for?
October 2025 to October 2026

Who is funding the study?
Asthma & Lung UK

Who is the main contact?
1. Dr Dean Fennell, df132@le.ac.uk
2. Dr Emma Knox, selectmeso1@soton.ac.uk

Contact information

Type(s)
Principal Investigator

Contact name
Dr Dean Fennell

Contact details
Room 539, 5th Floor
Robert Kilpatrick Building
Leicester
United Kingdom
LE2 7LX
-
df132@le.ac.uk

Type(s)
Scientific

Contact name
Dr Emma Knox

Contact details
Southampton Clinical Trials Unit
Centre for Cancer Immunology
Southampton General Hospital
Tremona Road
Southampton
United Kingdom
SO16 6YD
+44 (0)23 8120 4307
E.L.Knox@soton.ac.uk

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
1008628

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
RHMCAN1815, IRAS 1008628

Study information

Scientific Title
Platform: SynthEtic LEthal Cancer Therapy in mesothelioma (SELECTmeso): a molecularly stratified multi-arm Phase II platform trial for patients with relapsed malignant mesothelioma

Arm 1: A phase II trial of BMS-986504 in patients with MTAP-deficient relapsed mesothelioma

Acronym
SELECTmeso

Study objectives
Current study hypothesis as of 29/05/2025:

Primary objectives:
Platform: To determine the molecular subtype of mesothelioma to determine eligibility for SELECTmeso trial candidates which are open for recruitment.

SELECTmeso1: To determine the Disease Control Rate (DCR) of BMS-986504 at 12 weeks.

Secondary objectives:
Platform: To conduct in-depth molecular profiling of tumour blocks to enable exploration of the molecular determinants of sensitivity and acquired drug resistance.

SELECTmeso1: To determine DCR at 24 weeks, response rate, progression-free and overall survival (up to 24 weeks), safety and tolerability

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Previous study hypothesis:

Primary objectives:
Platform: To determine the molecular subtype of mesothelioma to determine eligibility for SELECTmeso trial candidates which are open for recruitment.

SELECTmeso1: To determine the Disease Control Rate (DCR) of brigimadlin (BI 907828) at 12 weeks.

Secondary objectives:
Platform: To conduct in-depth molecular profiling of tumour blocks to enable exploration of the molecular determinants of sensitivity and acquired drug resistance.

SELECTmeso1: To determine DCR at 24 weeks, response rate, progression-free and overall survival (up to 24 weeks), safety and tolerability

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 01/11/2024, South Central - Berkshire Research Ethics Committee (2 Redman Place, Stratford, E20 1JQ, United Kingdom; 02071048178; berkshire.rec@hra.nhs.uk), ref: 24/SC/0293

Study design
Non-randomized study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Safety, Efficacy

Participant information sheet

Not available in web format, please use the contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Relapsed malignant mesothelioma

Interventions
Current interventions as of 29/05/2025:

Mesothelioma patients with evidence of MTAP deficient relapsed mesothelioma on immunohistochemistry, and evidence of disease progression following prior standard systemic therapy.

Once all screening procedures have been completed and the patient is confirmed eligible they will start on trial IMP treatment. This trial is not randomised. Patients will be treated for up to 24 weeks or until disease progression, withdrawal, death or development of significant treatment-limiting toxicity. Patients will receive BMS-986504 orally at a dose of 600 mg four times a day continuously in 3 weekly cycles for up to 24 weeks.

During treatment, patients will be seen in clinic every 3 weeks for physical exams and blood tests to monitor safety. Patients will have a CT scan every 6 weeks from baseline, during treatment to assess their disease.

Following disease progression patients will be monitored for overall survival.

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Previous interventions:

Mesothelioma patients with evidence of MTAP loss and wild-type P53 on immunohistochemistry, and evidence of disease progression following prior standard systemic therapy.

Once all screening procedures have been completed and the patient is confirmed eligible they will start on trial IMP treatment. This trial is not randomised. Patients will be treated for up to 24 weeks or until disease progression, withdrawal, death or development of significant treatment-limiting toxicity. Patients will receive brigimadlin orally at a dose of 45 mg every 3 weeks for 24 weeks.

During treatment, patients will be seen in clinic every 3 weeks for physical exams and blood tests to monitor safety. Patients will have a CT scan every 6 weeks from baseline, during treatment to assess their disease.

Following disease progression patients will be monitored for overall survival.

Intervention Type
Drug

Pharmaceutical study type(s)
Pharmacodynamic, Pharmacogenetic, Pharmacogenomic

Phase

Phase II

Drug/device/biological/vaccine name(s)
BMS-986504

Primary outcome measure
Disease control rate assessed using mRECIST 1.1 for mesothelioma at 12 weeks

Secondary outcome measures
1. Disease control rate assessed using mRECIST 1.1 for mesothelioma at 24 weeks
2. Time-to-event data for overall survival (OS) and progression-free survival (PFS) up to 24 weeks will be presented using Kaplan-Meier curves. Median OS and PFS (with 95% confidence intervals) will be reported along with 12- and 24-week overall and progression-free survival. OS will also be collected up to 24 weeks plus 30 days.
3. Safety and tolerability reported in accordance with the NCI common terminology criteria for adverse events version 5. Adverse events will be collected up to 24 weeks plus 30 days.

Overall study start date
20/08/2024

Completion date
22/10/2026

Eligibility

Key inclusion criteria
Current inclusion criteria as of 29/05/2025:

Platform:
1. Histological confirmation of malignant mesothelioma (pleural, or non-pleural)
2. Evidence of disease progression on CT scan
3. Available archival tissue block for molecular screening
4. Previous treatment with at least 1st line licenced systemic anti-cancer therapy. Patients can have received more than one prior line of systemic therapy
5. No progressing CNS disease and not receiving any concurrent systemic therapy at the time of screening
6. ECOG performance status 0-1
7. 16 years of age and older
8. Expected survival of ≥12 weeks
9. Consent to provide baseline FFPE tumour tissue sample for trial
10. Patients must have signed and dated a REC-approved written informed consent form in accordance with regulatory and institutional guidelines. This must be obtained before the performance of any protocol-related procedures that are not part of normal patient care
11. Optional: Consent to store tissue for future research

SELECTmeso1:
1. Evidence of MTAP deficient relapsed mesothelioma
2. Willing to consent and able to undergo required procedures to provide blood
3. Adequate organ function, including the following:
3.1.. Adequate bone marrow reserve:
3.1.1. Absolute neutrophil count (ANC) ≥ 1.5 x 109/L

3.1.2. WBC ≥3 x 109/L
3.1.3. Haemoglobin ≥85 g/L
3.1.4. Platelet count ≥100 × 10e9/L
2. Adequate liver function and renal:
2.1. Bilirubin <1.5 x ULN
2.2. AST & ALT <3 x ULN
2.3. Creatinine clearance > 45 ml/min
3. INR ≤1.5 × institutional ULN unless on a stable dose of an anticoagulant with no unexplained elevation of INR
4. Participants must provide informed consent to SELECTmeso1 before any study specific procedures. The PI must confirm the eligibility of a participant in the participant's medical notes before enrolment.
5. 18 years of age and older

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Previous inclusion criteria:

Platform:
1. Histological confirmation of malignant mesothelioma (pleural, or non-pleural)
2. Evidence of disease progression on CT scan
3. Available archival tissue block for molecular screening
4. Previous treatment with at least 1st line licenced systemic anti-cancer therapy. Patients can have received more than one prior line of systemic therapy
5. ECOG performance status 0-1
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9. Patients must have signed and dated a REC-approved written informed consent form in accordance with regulatory and institutional guidelines. This must be obtained before the performance of any protocol-related procedures that are not part of normal patient care
10. Optional: Consent to store tissue for future research

SELECTmeso1:
1. Evidence of MTAP loss with wildtype p53
2. Willing to consent and able to undergo required procedures to provide blood
3. Adequate organ function, including the following:
3.1.. Adequate bone marrow reserve:
3.1.1. Absolute neutrophil count (ANC) ≥ 1.5 x 109/L
3.1.2. WBC ≥3 x 109/L
3.1.3. Haemoglobin ≥85 g/L
3.1.4. Platelet count ≥100 × 10e9/L
2. Adequate liver function and renal:
2.1. Bilirubin <1.5 x ULN
2.2. AST & ALT <3 x ULN
2.3. Creatinine clearance > 45 ml/min
3. INR ≤1.5 × institutional ULN unless on a stable dose of an anticoagulant with no unexplained elevation of INR
4. Participants must provide informed consent to SELECTmeso1 before any study specific procedures. The PI must confirm the eligibility of a participant in the participant's medical notes before enrolment.

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
30 Years

Sex
Both

Target number of participants
30

Key exclusion criteria
Current exclusion criteria as of 29/05/2025:

Platform:
1. No progressing CNS disease and not receiving any concurrent systemic therapy at the time of screening
2. Patients with a diagnosis of a second malignancy (except prostate or cervical cancer in remission, patients with a diagnosis of basal cell carcinoma or non-muscle invasive bladder cancer, who can all be included)
3. New York Heart Association Class II or greater congestive heart failure
4. Patients requiring long term oxygen therapy
5. Any other significant disease or disorder which, in the opinion of the investigator, may either put the participants at risk because of participation in the trial, or may influence the result of the trial, or the participants's ability to participate in the trial
6. Patients on active treatment in another clinical trial

SELECTmeso1:
1. MTAP-negative tumours not confirmed via IHC testing performed by the central lab.
2. Diagnosis, detection, or treatment of another type of cancer 5 years prior to initiating protocol therapy (except basal or squamous cell carcinoma of the skin, superficial non-muscle invasive bladder cancer that has been definitively treated), or prostate or cervical cancer in remission.
3. Have received treatment with an agent that has no marketing authorisation, within 14 days of study entry. If the patient has participated in a different SELECTmeso CST, they must comply with the washout period for that CST.
4. Patients of child-bearing potential who are not able to use at least one method of highly effective contraception (as detailed in section 5.3)
5. Patients who are pregnant or breast feeding
6. Uncontrolled CNS disease. Asymptomatic brain metastases are allowed if previously treated with radiotherapy >28 days prior to starting brigimadlin (BI 907828).
7. Palliative radiotherapy within the mRECIST 1.1 area in the 4 weeks prior to baseline CT scan.
8. Patients with severe hepatic insufficiency or severe renal impairment.
9. The patient has a personal history of any of the following conditions: syncope of

cardiovascular etiology, ventricular arrhythmia of pathological origin (including, but not limited to, ventricular tachycardia and ventricular fibrillation), or sudden cardiac arrest.
10. Patient has any of the following cardiac criteria:
10.1. Mean resting corrected QT interval (QTcF) >470 msec
10.2. Any clinically important abnormalities (as assessed by the investigator) in rhythm, conduction, or morphology of resting ECGs, e.g., complete left bundle branch block, third degree heart block
10.3. Any factors that increase the risk of QTc prolongation or risk of arrhythmic events such as heart failure, hypokalaemia, congenital long QT syndrome, family history of long QT syndrome or unexplained sudden death under 40 years of age, or any concomitant medication known to prolong the QT interval.
10.4. Ejection fraction (EF) <50% or the lower limit of normal of the institutional standard. Only in cases where the Investigator (or the treating physician or both) suspects cardiac disease with negative effect on the EF, will the EF be measured during screening using an appropriate method according to local standards to confirm eligibility (e.g., echocardiogram, multi-gated acquisition scan). A historic measurement of EF no older than 6 months prior to first administration of trial drug can be accepted provided that there is clinical evidence that the patient's cardiac disease has not significantly worsened since this measurement in the opinion of the Investigator or of the treating physician or both.
11. Active bleeding, significant risk of haemorrhage (e.g. previous severe gastrointestinal bleeding, previous haemorrhagic stroke at any time), or current bleeding disorder (e.g. haemophilia, von Willebrand disease.
12. All toxicities attributed to prior anti-cancer therapy not resolved to grade 1 or less before administration of study drug.
13. Major surgery, open biopsy or significant traumatic injury within 28 days before the start of study treatment or planned within 6 months after screening.
14. Any live vaccine within 30 days of consent.
15. Pre-existing duodenal stent and/or any gastrointestinal disorder or defect that would, in the opinion of the investigator, interfere with absorption of study treatment.
16. Previous significant surgical resection of stomach or small bowel.
17. Patients who have difficulty swallowing.
18. Patients who have received prior treatment with a PRMT5 inhibitor including BMS-986504, or MAT2A inhibitor.
19. Patients with active bacterial infection (requiring intravenous [IV] antibiotics at time of initiating study treatment), fungal infection, or detectable viral infection or viral load (such as known human immunodeficiency virus positivity or with known active hepatitis B or C [for example, hepatitis B surface antigen positive]. Screening is not required for enrolment.

20. Known severe hypersensitivity to study treatment and/or any of its excipients.

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Previous exclusion criteria:

Platform:
1. No progressing CNS disease and not receiving any concurrent systemic therapy at the time of screening
2. Patients with a diagnosis of a second malignancy (except prostate or cervical cancer in remission, patients with a diagnosis of basal cell carcinoma or non-muscle invasive bladder cancer, who can all be included)
3. New York Heart Association Class II or greater congestive heart failure
4. Patients requiring long term oxygen therapy

5. Any other significant disease or disorder which, in the opinion of the investigator, may either put the participants at risk because of participation in the trial, or may influence the result of the trial, or the participants's ability to participate in the trial
6. Patients on active treatment in another clinical trial

SELECTmeso1:
1. MTAP-negative tumours not confirmed via IHC testing performed by the central lab.
2. Diagnosis, detection, or treatment of another type of cancer 5 years prior to initiating protocol therapy (except basal or squamous cell carcinoma of the skin, superficial non-muscle invasive bladder cancer that has been definitively treated), or prostate or cervical cancer in remission.
3. Have received treatment with an agent that has no marketing authorisation, within 14 days of study entry. If the patient has participated in a different SELECTmeso CST, they must comply with the washout period for that CST.
4. Patients of child-bearing potential who are not able to use at least one method of highly effective contraception (as detailed in section 5.3)
5. Patients who are pregnant or breast feeding
6. Uncontrolled CNS disease. Asymptomatic brain metastases are allowed if previously treated with radiotherapy >28 days prior to starting brigimadlin (BI 907828).
7. Palliative radiotherapy within the mRECIST 1.1 area in the 4 weeks prior to baseline CT scan.
8. Patients with severe hepatic insufficiency or severe renal impairment.
9. The patient has a personal history of any of the following conditions: syncope of cardiovascular etiology, ventricular arrhythmia of pathological origin (including, but not limited to, ventricular tachycardia and ventricular fibrillation), or sudden cardiac arrest.
10. Patient has any of the following cardiac criteria:
10.1. Mean resting corrected QT interval (QTcF) >470 msec
10.2. Any clinically important abnormalities (as assessed by the investigator) in rhythm, conduction, or morphology of resting ECGs, e.g., complete left bundle branch block, third degree heart block
10.3. Any factors that increase the risk of QTc prolongation or risk of arrhythmic events such as heart failure, hypokalaemia, congenital long QT syndrome, family history of long QT syndrome or unexplained sudden death under 40 years of age, or any concomitant medication known to prolong the QT interval.
10.4. Ejection fraction (EF) <50% or the lower limit of normal of the institutional standard. Only in cases where the Investigator (or the treating physician or both) suspects cardiac disease with negative effect on the EF, will the EF be measured during screening using an appropriate method according to local standards to confirm eligibility (e.g., echocardiogram, multi-gated acquisition scan). A historic measurement of EF no older than 6 months prior to first administration of trial drug can be accepted provided that there is clinical evidence that the patient's cardiac disease has not significantly worsened since this measurement in the opinion of the Investigator or of the treating physician or both.
11. Active bleeding, significant risk of haemorrhage (e.g. previous severe gastrointestinal bleeding, previous haemorrhagic stroke at any time), or current bleeding disorder (e.g. haemophilia, von Willebrand disease.
12. All toxicities attributed to prior anti-cancer therapy not resolved to grade 1 or less before administration of study drug.
13. Major surgery, open biopsy or significant traumatic injury within 28 days before the start of study treatment or planned within 6 months after screening.
14. Any live vaccine within 30 days of consent.
15. Pre-existing duodenal stent and/or any gastrointestinal disorder or defect that would, in the opinion of the investigator, interfere with absorption of brigimadlin (BI 907828).
16. Previous significant surgical resection of stomach or small bowel.

17. Patients who have difficulty swallowing.
18. Patients who have received prior treatment with a MDM2-p53 antagonist including brigimadlin (BI 907828).
19. Patients with active bacterial infection (requiring intravenous [IV] antibiotics at time of initiating study treatment), fungal infection, or detectable viral infection or viral load (such as known human immunodeficiency virus positivity or with known active hepatitis B or C [for example, hepatitis B surface antigen positive]. Screening is not required for enrolment.

Date of first enrolment
22/10/2025

Date of final enrolment
22/10/2026

Locations

Countries of recruitment
United Kingdom

Study participating centre
Not provided at time of registration
United Kingdom
-

Sponsor information

Organisation
University of Southampton

Sponsor details
Ground Floor
Duthie Building
Mailpoint 138
Tremona Road
Southampton
England
United Kingdom
SO16 6YD
+44 (0)23 8120 5044
sponsor@uhs.nhs.uk

Sponsor type
University/education

Website

http://www.southampton.ac.uk/

ROR
https://ror.org/01ryk1543

Funder(s)

Funder type
Industry

Funder Name
Boehringer Ingelheim

Alternative Name(s)
Boehringer Ingelheim Pharmaceuticals, Inc., Boehringer Ingelheim International GmbH, BI, BIPI

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Publication and dissemination plan
1. Peer-reviewed scientific journals
2. Internal report
3. Conference presentation
4. Publication on website

To meet their ethical obligation to responsibly share data (and tissue samples) generated by clinical trials, SCTU operate a transparent data/sample sharing request process. As a minimum, anonymous data will be available for request from three months after publication of an article, to researchers who provide a completed Data Sharing request form that describes a methodologically sound proposal, for the purpose of the approved proposal and if appropriate a signed Data Sharing Agreement. Data will be shared once all parties have signed relevant data sharing documentation.

Intention to publish date
30/09/2027

Individual participant data (IPD) sharing plan

The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary

Data sharing statement to be made available at a later date